Minutes of Meeting

Alabama Medicaid Agency
Pharmacy and Therapeutics Committee

May 13, 2009

Attendees: Chairman Ben Main, Dr. Lucy Culpepper, Dr. Gerard J. Ferris, Dr. Michelle Freeman, Ms. Vicki Little Faulk, Dr. Kelli Littlejohn, Dr. Robert Moon, Ms. Latonage Porter, Dr. Chivers R. Woodruff and Dr. Tina Hisel

Absent: Dr. Nancy Sawyer, Dr. Joseph Thomas

1. OPENING REMARKS

Chairman Main called the Pharmacy and Therapeutics (P&T) Committee Meeting to order at 9:17 a.m.

2. APPROVAL OF MINUTES

Chairman Main asked if there were any corrections to the minutes from the February 11, 2009 P&T Committee Meeting.

There were no objections. Dr. Woodruff made a motion to approve the minutes as presented and Dr. Culpepper seconded to approve the minutes. The minutes were unanimously approved.

3. PHARMACY PROGRAM UPDATE

Dr. Littlejohn noted that a routine Preferred Drug List quarterly update was completed on April 1, 2009. On the same date, the Agency transitioned to a new Prior Authorization (PA) contractor, AQUAF, who will handle all PA requests with the exception of Pharmacy, Dental, Radiology, and Augmentative Communicator Devices. An alert has been sent to all providers.

In both March and April 2009, the Agency sent different alerts to pharmacy providers related to product selection codes (DAW codes) and correct prescriber numbers on pharmacy claims.

In response to the national public health alert related to the swine influenza, the Agency has extended the preferred status of Relenza® and Tamiflu® until further notice. The Agency will be monitoring this issue on a monthly basis through the CDC and the Alabama Department of Public Health.

During the Drug Utilization Review (DUR) meeting in April 2009, the DUR Committee recommended that the P&T Committee review methadone for potential PA due to safety concerns. Dr. Littlejohn read the formal DUR statement and explained that the Agency has asked the clinical contractor, Goold Health Systems (GHS), to perform a clinical review of methadone and bring their findings to the P&T Committee as soon as possible.

FDA is currently reviewing the safety of several opioids, including methadone, and will be hosting a series of meetings in May 2009. GHS will incorporate the recommendations from FDA into their clinical review and present the information to the P&T Committee. This will likely occur during the November 2009 meeting.

The Agency will be moving to a more streamlined, paperless system for manufacturer comments beginning with the August 2009 P&T Committee meeting. The manufacturer notification letter will be sent via e-mail. Therefore, it is important that manufacturers keep their contact information up-to-date. Allowances will be made for hard copies of the notification letter, if necessary. Manufacturer comment submissions will be accepted via e-mail in PDF format, allowing for increased efficiency in the review and approval process. Accepted comments will be sent electronically to P&T Committee members. Those members who do not use e-mail will continue to receive a hard copy of the comments via the postal service. The updated policy is available on the Medicaid website (www.medicaid.alabama.gov). For the August 2009 meeting, both a hard copy and electronic copy of the notification letter will be sent to manufacturers.

Dr. Littlejohn provided the Committee with a Positive Antipsychotic Management (PAM) update. Based on the recommendation of the P&T committee, a multi-stakeholder task force was created; members include Alabama-licensed child psychiatrists, pharmacists, and representatives from Alabama Medicaid Agency, Mental Health, Blue Cross Blue Shield and All Kids. The Agency is moving forward with the group's recommendation to utilize the current Comprehensive NeuroScience program (CNS) to address utilization of antipsychotic medication in children. Information regarding this initiative will be presented by Dr. Moon during the next Board of Medical Examiners meeting. A copy of the letter that will be sent to providers is available from Dr. Littlejohn. Dr. Moon commented that the situation in Alabama is not dissimilar to that in other States.

Dr. Littlejohn reminded the Committee that the P&T charge and reference documents, as well as skin and mucous membranes criteria were available in the clinical packet.

During the next P&T Committee meeting, members will have the option to attend via iLinc, a web conferencing service. The meeting will take place at the Medicaid building. There will be a web camera in the board room so that those members attending remotely can see the speakers. The clinical packet will be available online and a real time chat function will be available. Members will need a telephone and a computer with internet access and e-mail. The Agency has had success with iLinc in other meetings, particularly at the last two DUR Board meetings. Manufacturer speakers will be required to attend in person. SurveyMonkey will be used for voting.

Chairman Main commended the Agency for providing alternative meeting attendance capabilities. He stated that iLinc attendance is optional.

Chairman Main asked whether a psychiatric pediatrician would be involved in the educational efforts recommended by the PAM workgroup. Dr. Moon clarified that a board-certified child psychiatrist will be utilized, and the opportunity to participate has been offered to Alabama board-certified psychiatrists.

Dr. Moon stated that the Agency is trying to spread the news about PAM as broadly as possible by presenting to various groups; the goal is to increase awareness. He presented the PAM information during conferences in 2008 and will be presenting to the Community Mental Health Center on May 14, 2009. He will also speak at the Pediatric Association meeting this fall.

Chairman Main commended the Agency for taking the initiative to extend the PA on the medications used for the treatment of swine influenza.

4. ORAL PRESENTATIONS BY MANUFACTURERS/MANUFACTURERS' REPRESENTATIVES

There were no verbal presentations made on behalf of pharmaceutical manufacturers.

5. PHARMACOTHERAPY CLASS REVIEWS (Please refer to the website for full text reviews.)

The pharmacotherapy reviews began at approximately 9:35 a.m. The skin and mucous membrane classes were last reviewed in February 2007.

Skin and Mucous Membrane Antibacterials: American Hospital Formulary Service (AHFS) 840404
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane antibacterials are indicated for the treatment and prevention of various primary and secondary skin infections, as well as bacterial vaginosis. Table 1 provides a list of the products that are included in this review. Retapamulin is a new product that has become available since this class was last reviewed in 2007. However, this agent was reviewed as a new drug during the May 2008 P&T Committee meeting. The nasal formulation of mupirocin is no longer included in this AHFS subclass; this agent is now included in the EENT antibacterials class. Therefore, all references to nasal mupirocin product have been removed from this review. Products solely indicated for the treatment of acne and/or rosacea are not covered by Alabama Medicaid. Therefore, these products are not included in this review. Most of the antibacterials within this class are available in a generic formulation. Products containing bacitracin and polymyxin B, with or without neomycin, are also available over-the-counter.

Current treatment guidelines that incorporate the use of the antibacterials are summarized in Table 2. The guidelines have not been updated since this class was last reviewed. These guidelines include recommendations for the treatment of bacterial vaginosis, impetigo, and peritoneal dialysis-related infections. Guidelines for the management of bacterial vaginosis recommend initial treatment with either oral or vaginal metronidazole or clindamycin products. According to the IDSA guidelines on the management of skin and soft-tissue infections, the best topical agent for the treatment of impetigo is mupirocin. Topical antibacterials are effective in preventing exit-site infections in patients receiving peritoneal dialysis and the ISPD guidelines recommend either mupirocin ointment/cream or gentamicin cream daily after cleansing in all patients.
The FDA-approved indications for the skin and mucous membrane antibacterials are noted in Table 3. The pharmacokinetics, drug interactions, adverse events, as well as dosing and administration sections have been updated as necessary.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane antibacterials are summarized in Table 8. Several studies have demonstrated that prophylactic administration of topical antibacterials decreases infection rates in minor wounds. Bacitracin, neomycin, and polymyxin B prevented infections to a similar degree as monotherapy with mupirocin and bacitracin in patients with an uncomplicated soft tissue wound. Studies comparing topical mupirocin or retapamulin to oral antibiotics demonstrated similar clinical response rates. For the treatment of bacterial vaginosis, various metronidazole regimens have been

shown to be equally effective. Studies have shown that cure rates do not differ between intravaginal clindamycin cream and ovules. Several clinical trials have also demonstrated similar efficacy between metronidazole and clindamycin-containing treatment regimens. The topical antibacterials have been shown to be effective for the treatment of impetigo in several clinical trials. However, there are limited clinical trials comparing the various agents, and there are no published trials directly comparing retapamulin to mupirocin. Topical antibacterials are effective in preventing exit-site infections in patients receiving peritoneal dialysis. However, comparisons of different methods of exit-site care in randomized trials are limited.

Dr. Hisel concluded that the topical antibacterials are useful for preventing and treating a variety of skin infections. Treatment with the combination of bacitracin, neomycin, and polymyxin B prevented infections to a similar degree as monotherapy with mupirocin or bacitracin. Studies comparing mupirocin or retapamulin to oral antibiotics also demonstrated similar clinical response rates. For the treatment of bacterial vaginosis, guidelines recommend initial treatment with either metronidazole or clindamycin products. Various metronidazole regimens, as well as clindamycin regimens have been shown to be equally effective. For the treatment of impetigo, the IDSA guidelines state that the best topical agent is mupirocin. Other agents, such as bacitracin and neomycin, are less effective. The IDSA guidelines also state that topical therapy with mupirocin is equivalent to oral antimicrobials and may be used when lesions are limited in number. Retapamulin was not available when the IDSA guidelines were published in 2005. Therefore, there are no statements about the place in therapy for this agent. There are also no published trials directly comparing retapamulin to mupirocin. For the treatment of peritoneal dialysis-related infections, the ISPD guidelines recommend either topical mupirocin or gentamicin daily after cleansing in all patients.

Therefore, all brand skin and mucous membrane antibacterials within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane antibacterial is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee members to mark their ballots.

Skin and Mucous Membrane Antivirals: AHFS 840406
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane antivirals are used to treat herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), as well as external anogenital warts. The skin and mucous membrane antivirals that are included in this review are listed in Table 1. Sinecatechins is a new product that has become available since this class was last reviewed. Acyclovir and penciclovir are the only topical antiviral agents indicated for the treatment of herpes infections. Sinecatechins is the only topical antiviral agent indicated for the treatment of anogenital warts. No generic products are available in this class.

Current treatment guidelines that incorporate the use of the skin and mucous membrane antivirals are summarized in Table 2. The British Association for Sexual Health and HIV guidelines for the Management of Genital Herpes have been added to the clinical packet. These guidelines state that topical agents are less

effective than oral agents for the treatment of genital herpes and combined oral and topical treatment is of no benefit. The other guidelines have not changed since the last review.

The FDA-approved indications for the skin and mucous membrane antivirals are listed in Table 3. Acyclovir is indicated for both genital and labial herpes infections; whereas, penciclovir is only indicated for the treatment of recurrent herpes labialis. The pharmacokinetics, drug interactions, adverse drug events, as well as dosing and administration sections have been updated as necessary.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane antivirals are summarized in Table 7. Both acyclovir and penciclovir have been shown to be more effective than placebo for the treatment of genital herpes. Only one study (Chen et al.) directly compared these two agents, which demonstrated similar efficacy. For the treatment of recurrent herpes labialis, both acyclovir and penciclovir have been shown to decrease lesion healing time and duration of pain compared to placebo. Two studies directly compared acyclovir and penciclovir for the treatment of herpes labialis. In a study conducted by Femiano et al., penciclovir resulted in a quicker time to crusting and cessation of pain compared to acyclovir; however, there was no significant difference in time to healing. In a second study conducted by Lin et al., acyclovir and penciclovir demonstrated similar efficacy in clinical cure rates and time to healing. Only one published clinical trial with sinecatechins was found in the medical literature. This study demonstrated that 57% of patients treated with sinecatechins had complete clearance of their external anogenital warts compared to 33% of placebo-treated patients

Dr. Hisel concluded that the skin and mucous membrane antivirals are approved for the treatment of herpes simplex virus infections and external anogenital warts. Guidelines on the management of genital herpes state that topical antiviral agents are less effective than oral agents, offer minimal clinical benefits and do not recommend their use for this indication. Only acyclovir ointment is FDA-approved for the treatment of genital herpes. One study directly compared acyclovir and penciclovir for the treatment of genital herpes, which demonstrated similar efficacy among the agents. There are no published guidelines on the management of labial herpes. Both acyclovir and penciclovir have been shown to decrease lesion healing time and duration of pain compared to placebo. Although the results were statistically significant, the clinical significance is unknown. Healing times and duration of pain were only reduced by one day, or less, compared to placebo. Two studies directly compared acyclovir and penciclovir; in the first study, penciclovir resulted in a quicker time to crusting and cessation of pain compared to acyclovir. In a second study, acyclovir and penciclovir demonstrated similar efficacy. Guidelines on the management of anogenital warts state that there is no definitive evidence to suggest that any of the available treatments are superior to any other and no single treatment is ideal for all patients or all warts. Only one published clinical trial with sinecatechins was found in the medical literature, demonstrating greater clearance of warts compared to placebo. There are no published clinical trials comparing sinecatechins to other treatment options for anogenital warts.

Therefore, all brand skin and mucous membrane antivirals within the class reviewed are comparable to each other and to the generics (if applicable) and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane antiviral is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There was no further discussion on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Antifungals: AHFS 840408
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane antifungals are used to treat a variety of fungal infections, including cutaneous and oropharyngeal candidiasis, vulvovaginal candidiasis, seborrheic dermatitis, onychomycosis and dermatophyte infections. The antifungals that are included in this review are listed in Table 1. Many of these agents are available in a generic formulation. Clotrimazole, miconazole, terbinafine, tioconazole and tolnaftate are also available over-the-counter.

Current treatment guidelines that incorporate the use of the skin and mucous membrane antifungals are summarized in Table 2. Two guidelines have been added since this class was last reviewed. The ACOG guidelines on vaginitis list a variety of topical antifungal agents that can be used and state that they seem to have comparable safety and efficacy. Therefore, the choice of therapy should be individualized to the specific patient; factors such as ease of use, history of response or adverse reactions to prior treatments, and patient preference should be taken into consideration. The Finnish Medical Society guidelines on seborrheic dermatitis recommend washing the scalp with ketoconazole or selenium sulphide shampoo as well as topical treatment with creams containing imidazole derivatives to decrease fungal growth. The other guidelines have not been updated since this class was last reviewed.

The FDA-approved indications for the skin and mucous membrane antifungals are noted in Table 3; the indications vary by drug and formulation. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption with the skin and mucous membrane antifungals, no significant drug interactions have been reported.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane antifungals are summarized in Table 8. For the treatment of candidal skin infections, studies have reported similar efficacy with clotrimazole and nystatin, with nystatin monotherapy and the nystatin/triamcinolone combination product, as well as with sulconazole and miconazole. For the treatment of oropharyngeal candidiasis, two clinical trials reported that clotrimazole troches were associated with significantly greater improvement in both clinical and mycological response in oropharyngeal candidiasis compared to placebo. For the treatment of vulvovaginal candidiasis, numerous clinical trials have demonstrated similar efficacy among various topical imidazole antifungal agents. For the treatment of seborrheic dermatitis, ciclopirox demonstrated significant improvements in clinical cure rates compared to placebo. Ketoconazole demonstrated significant improvements in clinical cure rates compared to placebo and zinc pyrithione. For the treatment of onychomycosis, treatment with ciclopirox has led to improvements in clinical and mycological cure rates in two clinical trials. For the treatment of tinea infections, numerous studies have demonstrated similar efficacy among the various topical antifungal agents. Two studies found that the combination product containing clotrimazole and betamethasone was more effective than monotherapy with either clotrimazole or betamethasone alone.

Dr. Hisel concluded that the skin and mucous membrane antifungal agents are effective treatments for a variety of fungal infections. Guidelines for the treatment of candidal skin infections state that topical imidazoles and polyenes are effective treatment options and clinical studies have demonstrated similar efficacy among several products. Guidelines for the treatment of oropharyngeal candidiasis state that topical and oral imidazoles or oral polyenes are effective treatment options. Initial episodes can be treated with clotrimazole troches or oral nystatin. In refractory or recurrent cases, oral and intravenous antifungal agents are recommended. The clotrimazole troche is the only skin and mucous membrane antifungal indicated for the treatment of oropharyngeal candidiasis and it has been shown to be more effective than placebo. Several guidelines on the

management of vulvovaginal candidiasis (VVC) have been published and recommend the use of the topical antifungal agents as initial therapy. They do not give preference to one antifungal agent over another. Numerous clinical trials have demonstrated similar efficacy among various topical imidazole antifungal agents. However, studies have shown that the imidazoles are more effective than nystatin. Guidelines for the treatment of seborrheic dermatitis are limited; however, one organization recommends ketoconazole shampoo and topical imidazole creams to decrease fungal growth. Ciclopirox and ketoconazole have both improved clinical cure rates in clinical trials. There were no published studies found in the medical literature directly comparing these two agents. There were also no published studies found evaluating the dual use of ketoconazole gel and pyrithione zinc shampoo. Guidelines for the treatment of onychomycosis state that systemic therapy is almost always more successful than topical treatment. Treatment with ciclopirox has led to improvements in clinical and mycological cure rates in clinical trials. There are no current treatment guidelines that specifically address the management of tinea infections. Numerous studies have demonstrated similar efficacy among the various topical antifungal agents. Two studies found that the combination product containing clotrimazole/betamethasone was more effective than monotherapy with either clotrimazole or betamethasone. However, there were no published studies directly comparing the clotrimazole/betamethasone combination product to dual therapy with clotrimazole and betamethasone as separate formulations. There were no published clinical trials found in the medical literature evaluating the safety and efficacy of the sodium thiosulfate/salicylic acid combination product. For the treatment of diaper dermatitis, two studies demonstrated greater clinical cure the miconazole/zinc oxide combination product compared to monotherapy with zinc oxide. However, there were no studies directly comparing the miconazole/zinc oxide combination product to dual therapy with miconazole and zinc oxide as separate formulations.

Therefore, all brand skin and mucous membrane antifungals within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane antifungal is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Dr. Woodruff asked if any of the studies addressed resistance with the over-the-counter (OTC) antifungal agents for the treatment of tinea infections. Dr. Hisel commented that none of the studies included in the clinical packet directly addressed resistance with the OTC antifungal agents. She stated that there were very few new studies published for this indication. Dr. Woodruff stated that he was concerned that patients would have to fail OTC therapies before receiving approval for a prescription antifungal agent. Dr. Littlejohn commented that there are several prescription antifungal agents that are currently preferred, and clarified that prior therapies may be any prescribed and preferred agent, whether legend or OTC.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Scabicides and Pediculicides: AHFS 840412
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane scabicides and pediculicides are used to treat scabies and pediculosis. The agents that are included in this review are listed in Table 1. Crotamiton is the only agent that is not available in a generic formulation. Malathion was recently approved by the FDA as a new generic

formulation. Lindane is available in a generic formulation; however, due to safety concerns with the use of this agent, the P&T Committee recommended that generic lindane products be made non-preferred. Therefore, prior authorization is required for the use of lindane.

Current treatment guidelines that incorporate the use of the skin and mucous membrane scabicides and pediculicides are summarized in Table 2. Two guidelines have been added to the clinical packet, which were released by the British Association of Sexual Health and HIV. The guideline on the management of scabies and the guideline on the management of pediculosis pubis recommend treatment with permethrin or Malathion. The CDC guidelines have not changed since this class was last reviewed. The CDC recommends permethrin or oral ivermectin for treatment of scabies and permethrin or piperonyl butoxide/pyrethrins for the treatment of pediculosis pubis. There were no guidelines found discussing the management of head lice.

The FDA-approved indications for the skin and mucous membrane scabicides and pediculicides are noted in Table 3. According to the prescribing information, lindane should only be used in patients who cannot tolerate or have failed first-line treatment with safer medications. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. There are no significant drug interactions with the skin and mucous membrane scabicides and pediculicides. However, lindane should be used with caution with any drug that is known to lower the seizure threshold. The boxed warning for lindane is listed in Table 6. It states that seizures and deaths have been reported following lindane use with repeat or prolonged application, but also in rare cases following a single application according to directions. Lindane should be used with caution in infants, children, the elderly, and individuals with other skin conditions, and those who weigh <110 lbs (50 kg) as they may be at risk for serious neurotoxicity.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane scabicides and pediculicides are summarized in Table 8. For the treatment of scabies, several clinical trials have demonstrated greater efficacy with permethrin compared to lindane or crotamiton. Only one published study evaluated the use of topical pediculicides for the treatment of pediculosis pubis. Kalter et al. demonstrated similar efficacy with the use of lindane and permethrin. For the treatment of head lice, several clinical trials have demonstrated greater efficacy with permethrin compared to lindane and piperonyl butoxide /pyrethrins. Malathion was shown to be more effective than permethrin in two clinical trials. However, both studies were conducted in the same study population in South Florida. The authors noted that observations from over 12 years suggest the presence of pesticide-resistant lice in this population.

Dr. Hisel concluded that the skin and mucous membrane scabicides and pediculicides are effective treatment options for scabies and pediculosis of the head, body and pubic region. The CDC guidelines on the management of scabies recommend initial treatment with either permethrin or ivermectin. Lindane is considered an alternative treatment option. Several clinical trials have demonstrated greater efficacy with permethrin compared to lindane or crotamiton. The CDC guidelines for the treatment of pediculosis pubis recommend permethrin or piperonyl butoxide/pyrethrins. Alternative treatments include malathion or ivermectin. Malathion may be used when treatment failure is believed to have occurred because of resistance. Only one published study evaluated the use of topical pediculicides for the treatment of pediculosis pubis and demonstrated similar efficacy with the use of lindane and permethrin. There were no guidelines found discussing the management of head lice. The American Academy of Pediatrics recommends permethrin as the initial treatment. None of the available pediculicides are 100% ovicidal and resistance has been reported with lindane, pyrethrins and permethrin. Several clinical trials have demonstrated greater efficacy with permethrin compared to lindane and piperonyl butoxide/pyrethrins.

Potential adverse events limit the use of some of these agents. Seizures and deaths have been reported following lindane use. Lindane is not recommended as first-line therapy because of toxicity. Malathion is an organophosphate agent and is flammable; the lotion and hair wet with lotion should not be exposed to open flames or electric heat sources, including hair dryers and electric curlers. Patients should not smoke while applying the lotion or while the hair is wet.

Therefore, all brand skin and mucous membrane products within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use. Lindane possesses an extensive adverse effect profile compared to the other brands, generics and OTC products in the class.

No brand skin and mucous membrane scabicide or pediculicide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Lindane should not be placed in preferred status regardless of cost.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Local Anti-infectives, Miscellaneous: AHFS 840492
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane miscellaneous local anti-infectives have a variety of uses, including treatment of vaginal infections, antiseptic cleansing, and prevention/treatment of burn wounds. The agents included in this review are listed in Table 1. Sulfanilamide is used for the treatment of vulvovaginal candidiasis. Acetic acid and oxyquinoline (with or without ricinoleic acid) is used as an adjunctive therapy when restoration and maintenance of vaginal acidity is desired, such as in bacterial vaginosis. Hexachlorophene is a bacteriostatic cleansing agent. Mafenide, silver nitrate and silver sulfadiazine are used for the prevention and treatment of burn wound infections and all three have a broad spectrum of activity. Several products are available in a generic formulation with the exception of hexachlorophene, mafenide, and sulfanilamide. Products indicated solely for the treatment of acne and/or rosacea is not covered by Alabama Medicaid. Therefore, these products are not included in this review.

Current treatment guidelines that incorporate the use of the skin and mucous membrane miscellaneous local anti-infectives are summarized in Table 2. The only guidelines that are available discuss the treatment of vaginitis and hand hygiene. These guidelines have not changed since this class was last reviewed.

The FDA-approved indications for the skin and mucous membrane miscellaneous local anti-infectives are noted in Table 3. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption with the skin and mucous membrane miscellaneous local anti-infectives, no significant drug interactions have been reported.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane miscellaneous local anti-infectives are summarized in Table 7. Studies evaluating hexachlorophene as a hygienic hand wash and surgical scrub demonstrated only modest efficacy after a single handwash. There are very few clinical trials directly comparing mafenide, silver nitrate and silver sulfadiazine for the prevention and treatment of burn wounds.

MacMillan et al. reported similar efficacy with mafenide and silver nitrate in patients with second-and third-degree burn wounds requiring topical antibacterial therapy. Pegg et al. demonstrated similar efficacy with mafenide and silver sulfadiazine in patients with burn injuries requiring admission. There were no published clinical trials found in the medical literature with acetic acid/oxyquinoline (with or without ricinoleic acid) or sulfanilamide.

Dr. Hisel concluded that the skin and mucous membrane miscellaneous local anti-infectives have a variety of uses, including treatment of vaginal infections, antiseptic cleansing, and prevention/treatment of burn wounds. Current guidelines on the management of vaginal infections do not specifically mention or recommend the use of acetic acid/oxyquinoline or sulfanilamide. There were no published clinical trials found in the medical literature with these agents. Hexachlorophene is a bacteriostatic cleansing agent which is FDA-approved for use as a surgical scrub and a bacteriostatic skin cleanser. The CDC guidelines on hand hygiene in health care settings recommend alcohol-based products for standard handwashing or hand antisepsis compared to soap or antimicrobial soaps as they are more effective. Studies of hexachlorophene as a hygienic hand wash and surgical scrub demonstrated only modest efficacy after a single handwash. With repeated use, hexachlorophene is absorbed through the skin. As a result, it is seldom used as a surgical scrub. Hexachlorophene should not be used to bathe patients with burns or extensive areas of susceptible, sensitive skin. Current guidelines recommend against the routine bathing of neonates with hexachlorophene because of its potential neurotoxic effects. There were no published guidelines found discussing the use of the miscellaneous local anti-infective agents for the treatment of burn wounds, and there are very few clinical trials directly comparing the agents. Silver sulfadiazine is the most frequently used agent because of its low toxicity and ease of use. Mafenide rapidly penetrates burn eschar; however, the application must be limited because of systemic toxicity associated with prolonged or extensive use. Silver nitrate does not penetrate the eschar due to precipitation upon contact with exudates. It is only used for prevention of infection and is not effective in treating wound infections. Silver nitrate may be an effective treatment option for patients with an allergy to sulfonamides.

Therefore, all brand skin and mucous membrane miscellaneous local anti-infective products within the class reviewed are comparable to each other and to the generics in the class and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane miscellaneous local anti-infective is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Anti-inflammatory Agents: AHFS 840600
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane anti-inflammatory agents are indicated for the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. This includes anogenital pruritus, atopic dermatitis, localized neurodermatitis, psoriasis, seborrheic dermatitis, and the inflammatory phase of xerosis. The agents that are included in this review are listed in Table 1. The topical corticosteroids are classified based on their relative potency and the potency categories are listed in Table 2. There is at least one topical corticosteroid from each potency category available in a generic formulation. Hydrocortisone is also available in various formulations over-the-counter.

Current treatment guidelines that incorporate the use of the skin and mucous membrane anti-inflammatory agents are summarized in Table 3. The American Academy of Dermatology guidelines for the management of psoriasis with topical therapies were recently updated and state that topical corticosteroids are the standard of care. The Finnish Medical Society guidelines on the treatment of seborrhoeic dermatitis have been added to the clinical packet and recommend the use of corticosteroids for symptomatic topical treatment. The other guidelines have not been updated since this class was last reviewed.

The FDA-approved indications for the skin and mucous membrane anti-inflammatory agents are noted in Table 4. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption with the skin and mucous membrane anti-inflammatory agents, no significant drug interactions have been reported. Several topical anti-inflammatory agents are approved for use in pediatric patients. Desonide, fluocinolone, and fluticasone may be used in children as young as 3 months old. Alclometasone is approved for children as young as 1 year of age and mometasone is approved for children as young as 2 years of age. A variety of other products do no specifically list age limits in the pediatric population.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane anti-inflammatory agents are summarized in Table 8. Numerous clinical trials have demonstrated similar efficacy among the various topical corticosteroids for the treatment of atopic dermatitis, psoriasis, and seborrheic dermatitis.

Dr. Hisel concluded that the skin and mucous membrane anti-inflammatory agents are indicated for the treatment of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Guidelines for the management of atopic dermatitis and psoriasis state that topical corticosteroids are the standard of care and do not give preference to one agent over another. Selection of the topical corticosteroid should take into account the disease severity, location of the lesions, patient's age, and anticipated duration of therapy. Numerous clinical trials have demonstrated similar efficacy among the various topical corticosteroids for the treatment of atopic dermatitis and psoriasis. Some clinical trials have demonstrated greater efficacy with one agent over another; however, these studies were comparing corticosteroids with different potencies. Topical corticosteroids are just one of many treatment options for seborrheic dermatitis. Guidelines recommend liquid preparations for the scalp and creams for other parts of the body. Guidelines for the treatment of hemorrhoids state that the cornerstone of therapy is adequate fiber intake and water. Corticosteroid creams may ameliorate local perianal inflammation, but no data suggest that they actually reduce hemorrhoidal swelling, bleeding, or protrusion. Over-the-counter topical agents and suppositories are often used in the empirical treatment of hemorrhoids, however data supporting their use is lacking.

Therefore, all brand skin and mucous membrane anti-inflammatory products within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over the other alternatives in general use.

No brand skin and mucous membrane anti-inflammatory agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Antipruritics and Local Anesthetics: AHFS 840800
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane antipruritics and local anesthetics have a variety of indications, including relief of itching and pain caused by insect bites, minor burns, sunburns, atopic dermatitis, eczema, lichen simplex chronicus, and hemorrhoids. They are also used to prevent and treat pain due to postherpetic neuralgia, minor operative/dermatological procedures, endoscopic/diagnostic procedures, venipuncture, intravenous cannulation, as well as other procedures. The skin and mucous membrane antipruritics and local anesthetics that are included in this review are listed in Table 1. Several antipruritic and local anesthetic products are available in a generic formulation. Pramoxine is also available over-the-counter.

Current treatment guidelines that incorporate the use of the skin and mucous membrane antipruritics and local anesthetics are summarized in Table 2. These guidelines provide recommendations for the treatment of atopic dermatitis, hemorrhoids, and postherpetic neuralgia; however they have not been updated since this class was last reviewed.

The FDA-approved indications for the skin and mucous membrane antipruritics and local anesthetics are noted in Table 3. The pharmacokinetics, drug interactions, adverse drug events, as well as dosing and administration sections have been updated as necessary. FDA issued a public health advisory to remind patients, healthcare professionals, and caregivers about potentially serious hazards of using topical anesthetics for relieving pain from medical tests and conditions. FDA remains concerned about the potential for topical anesthetics to cause serious and life-threatening adverse effects when applied to a large area of skin or when the area of application is covered. Skin temperature can increase during exercise, by covering the skin with a wrap, or with use of a heating pad. Under these circumstances, the amount of topical anesthetic that reaches the systemic circulation is unpredictable and may be high enough to cause life-threatening adverse effects such as arrhythmias, seizures, respiratory difficulties, coma and death.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane antipruritics and local anesthetics are summarized in Table 8. One study demonstrated that topical doxepin was more effective than placebo at controlling pruritus over the course of 7 days. Two clinical trials evaluated the use of ethyl chloride spray as an anesthetic prior to intravenous (IV) cannulation. Ramsook et al. reported no significant difference in pain scores compared to isopropyl alcohol and Robinson et al. reported that intradermal lidocaine was significantly more effective than ethyl chloride at reducing the pain of IV cannulation. Numerous clinical trials have found lidocaine, lidocaine/prilocaine, lidocaine/tetracaine, and pramoxine to be more effective than placebo at relieving pain. There are few clinical trials directly comparing the topical anesthetics. Comparative studies found no differences in pain relief with lidocaine and lidocaine/prilocaine preparations.

Dr. Hisel concluded that the skin and mucous membrane antipruritics and local anesthetics have a variety of indications, including relief of itching and pain caused by insect bites, minor burns, sunburns, atopic dermatitis, eczema, lichen simplex chronicus, and hemorrhoids. They are also used to prevent and treat pain due to postherpetic neuralgia, minor operative/dermatological procedures, endoscopic/diagnostic procedures, venipuncture, intravenous cannulation, as well as other procedures. Due to the variety of products, dosage forms and FDA-approved indications, direct comparisons of agents within this class is difficult. There are also few clinical guidelines that discuss the use of these agents. The American Academy of Dermatology guidelines on atopic dermatitis state that topical corticosteroids are the standard of care and that the short-term use of topical doxepin may relieve pruritus; however, adverse events limit its usefulness. Guidelines for the treatment of hemorrhoids state that the cornerstone of therapy is adequate fiber intake and water. Topical corticosteroids and

analgesics are useful for managing perianal skin irritation. A literature search did not reveal any published studies evaluating the use of lidocaine/hydrocortisone combination products for the treatment of hemorrhoids or other disorders. There are no treatment guidelines that specifically discuss the use of topical local anesthetics for pain relief. Numerous clinical trials have found these agents to be more effective at relieving pain than placebo. However, there are few clinical trials directly comparing the topical local anesthetics. Comparative studies found no differences in pain relief with several different formulations of lidocaine and lidocaine/prilocaine products. A literature search did not reveal any published studies evaluating the use of benzocaine 20% lubricant or tetracaine 2% solution.

FDA remains concerned about the potential for topical anesthetics to cause life-threatening adverse events such as arrhythmias, seizures, respiratory difficulties, coma and death. If a topical anesthetic is prescribed, patients should use the least amount that will relieve the pain, apply the product sparingly, and do not apply the product to broken or irritated skin.

Therefore, all brand skin and mucous membrane antipruritic and local anesthetic products within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane antipruritic or local anesthetic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

At 10:19, Chairman Main asked if the Committee wanted to take a break; the Committee declined.

Skin and Mucous Membrane Astringents: AHFS 841200
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that aluminum chloride is the only skin and mucous membrane astringent in the class and it is FDA-approved for the treatment of hyperhidrosis. It is also available in a generic formulation.

There are limited guidelines on the treatment of hyperhidrosis. The International Hyperhidrosis Society guidelines state that topical aluminum chloride antiperspirants are the first-line treatment for hyperhidrosis. If a patient does not adequately respond to topical antiperspirant therapy or if the side effects are intolerable, botulinum toxin A, systemic medications, and surgery are also treatment options.

The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption, no significant drug interactions have been reported with aluminum chloride.

Clinical studies evaluating the safety and efficacy of aluminum chloride are summarized in Table 7. Although aluminum chloride has been available for many years, there are very few clinical trials assessing the efficacy and safety of this agent. It has been shown to be effective in reducing axillary and palmar hyperhidrosis; however, clinical trials have enrolled small numbers of patients. Flanagan et al. compared treatment with aluminum chloride and botulinum toxin type A (BTX-A) in patients with moderate to severe axillary

hyperhidrosis. BTX-A was more effective than aluminum chloride at week 4 and provided greater patient satisfaction. Rayner et al. reported that, after 6 months of treatment with aluminum chloride, 68% of study patients opted for surgery.

Dr. Hisel concluded that topical aluminum chloride antiperspirants are the first-line treatment for axillary, palmar and plantar hyperhidrosis. Although aluminum chloride has been available for many years, there are very few clinical trials assessing the efficacy and safety of this agent. Aluminum chloride has been shown to be an effective treatment option for hyperhidrosis. Nightly application is effective and once excessive sweating is controlled, treatment frequency can be reduced to once or twice weekly as needed. The use of aluminum chloride is often associated with skin irritation, but this may be managed by applying the product on dry skin at bedtime and washing it off in the morning. Aluminum chloride is the only agent in this class and is available in a generic formulation.

Therefore, all brand skin and mucous membrane astringents within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane astringent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Keratolytic Agents: AHFS 842800
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane keratolytic agents are used to treat a variety of hyperkeratotic skin conditions, including psoriasis, xerosis, ichthyosis, eczema, corns, calluses, cutaneous verrucae, as well as others. They are also used for the treatment of damaged, ingrown, and devitalized nails. The skin and mucous membrane keratolytic agents that are included in this review are listed in Table 1, which include salicylic acid and urea. Both agents are available in a generic formulation. Products solely indicated for the treatment of acne and/or rosacea is not covered by Alabama Medicaid. Therefore, these products are not included in this review.

Current treatment guidelines that incorporate the use of the skin and mucous membrane keratolytic agents are summarized in Table 2. These guidelines provide recommendations on the treatment of psoriasis, seborrheic dermatitis, and cutaneous warts. The American Academy of Dermatology guidelines for the management of psoriasis have been recently updated. These guidelines state that topical corticosteroids are the cornerstone of treatment for the majority of patients with psoriasis. They also mention that while there are no placebo-controlled studies verifying the efficacy and safety of salicylic acid used alone in the treatment of psoriasis, salicylic acid is often combined with other topical therapies. The improvements in efficacy of combination therapy are likely due to the increased skin penetration that occurs because of the keratolytic effects of salicylic acid. The Finnish Medical Society guidelines on seborrheic dermatitis have been added to the clinical packet. These guidelines state that the scales can be softened with a salicylic acid-containing product. The other guidelines have not been updated since this class was last reviewed.

The FDA-approved indications for the skin and mucous membrane keratolytic agents are noted in Table 3. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption with the skin and mucous membrane keratolytics, no significant drug interactions have been reported.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane keratolytic agents are summarized in Table 7. Although the keratolytic agents have been available for many years, there are limited clinical trials evaluating the use of salicylic acid (6%) and urea (30% - 50%). The available studies have been of short duration and included small numbers of patients. There are no studies directly comparing salicylic acid and urea.

Dr. Hisel concluded that salicylic acid and urea are used to treat a variety of hyperkeratotic skin conditions, including psoriasis, xerosis, ichthyosis, eczema, corns and calluses. Salicylic acid is also indicated for the treatment of cutaneous verrucae. Urea is also indicated for the treatment of damaged, ingrown, and devitalized nails. Both agents are generally well tolerated, with side effects limited to local skin reactions. There are very few guidelines available which discuss the use of salicylic acid or urea for the treatment of hyperkeratotic skin conditions. Guidelines for the management of psoriasis recommend salicylic acid as one of many treatment options. Salicylic acid is also recommended for treating seborrheic dermatitis to help soften scales. The guidelines for the management of cutaneous warts state that there is no single treatment that is 100% effective. Salicylic acid is one of many treatment options; however, there is not enough evidence to conclude that other therapies are more effective than salicylic acid. There is no mention of urea in the available clinical guidelines.

Therefore, all brand skin and mucous membrane keratolytic agents within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane keratolytic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Keratoplastic Agents: AHFS 843200
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the skin and mucous membrane keratoplastic agents are used to treat psoriasis, seborrheic dermatitis and dandruff. The agents that are included in this review are listed in Table 1 and include anthralin and coal tar. Coal tar is available in a generic formulation and is also available over-the-counter.

Current treatment guidelines that incorporate the use of the skin and mucous membrane keratoplastic agents are summarized in Table 2. These guidelines provide recommendations for the treatment of psoriasis and seborrheic dermatitis. The American Academy of Dermatology guidelines for the management of psoriasis have been recently updated. These guidelines state that topical corticosteroids are the cornerstone of treatment for the majority of patients with psoriasis. Coal tar products are often poorly tolerated by patients because of cosmetic issues, including staining of clothes and the tar odor that is present in almost all products. The guidelines also state that anthralin appears to have lower efficacy than more potent topical corticosteroids or vitamin D derivatives.

The FDA-approved indications for the skin and mucous membrane keratoplastic agents are noted in Table 3. The pharmacokinetics, adverse drug events, as well as dosing and administration sections have been updated as necessary. Due to limited systemic absorption with the skin and mucous membrane keratoplastic agents, no significant drug interactions have been reported.

Clinical studies evaluating the safety and efficacy of the skin and mucous membrane keratoplastic agents are summarized in Table 7. Although coal tar and anthralin have been available for many years, there are limited clinical trials evaluating the efficacy and safety of these agents directly or compared to placebo.

Dr. Hisel concluded that coal tar is indicated for the treatment of psoriasis, seborrheic dermatitis and dandruff, whereas anthralin is only indicated for the treatment of psoriasis. Guidelines for the treatment of psoriasis state that topical corticosteroids are the cornerstone of treatment for the majority of patients. Guidelines for the treatment of seborrheic dermatitis state that topical corticosteroids, antifungal agents and moisturizing emollients are the standard of care. Both coal tar and anthralin have been shown to be effective treatment options. Although they have been available for many years, there are limited clinical trials evaluating the efficacy and safety of these agents directly or compared to placebo. Coal tar products are often poorly tolerated because of staining and the tar odor. It is carcinogenic in animals; however, in humans, there is no firm evidence to indicate that it causes cancer. Anthralin causes skin irritation and staining of skin, nails and clothing. There is no evidence to suggest any long-term local or systemic toxicity with the use of anthralin.

Therefore, all brand skin and mucous membrane keratoplastic agents within the class reviewed are comparable to each other and to the generics and OTC products in the class and offer no significant clinical advantage over other alternatives in general use.

No brand skin and mucous membrane keratoplastic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

Skin and Mucous Membrane Agents, Miscellaneous: AHFS 849200
Manufacturer comments on behalf of these products:
None

Dr. Hisel commented that the miscellaneous skin and mucous membrane class includes a diverse group of products used to treat many skin conditions, including actinic keratoses, atopic dermatitis, basal cell carcinoma, cutaneous T-cell lymphoma, anogenital warts, hemorrhoids, Kaposi's sarcoma, psoriasis, and wounds. The agents included in this review are listed in Table 1. Acitretin is an oral formulation that is packaged with emollient foam. The other agents in this review are topical formulations. Acitretin and the thrombin, fibrinogen, aprotinin, and calcium chloride kit are new products since this class was last reviewed. Calcipotriene, fluorouracil, and podofilox are available in a generic formulation. The combination products containing phenylephrine, shark liver oil and white petrolatum with either glycerin or mineral oil are also available in a generic formulation as well as over-the-counter. The papain-containing products have been removed from the clinical packet. FDA ordered companies to stop manufacturing unapproved drug products that contain papain in a topical dosage form in November 2008. Currently, there are no FDA-approved topical drug products containing papain on the market.

Current treatment guidelines that incorporate the use of the miscellaneous skin and mucous membrane agents are summarized in Table 2. Three guidelines have been updated since this class was last reviewed. The British Association of Dermatologists guidelines for the management of actinic keratoses state that diclofenac, fluorouracil and imiquimod treatments are all effective and do not give preference to one agent over another. The National Comprehensive Cancer Network guidelines on basal cell and squamous cell skin cancers state that in patients with low-risk squamous cell carcinoma in situ, where surgery or radiation is contraindicated or impractical, topical therapies such as 5-fluorouracil, imiquimod, and photodynamic therapy may be considered even though cure rate may be lower. The American Academy of Dermatology guidelines for the management of psoriasis with topical therapies state that topical corticosteroids are the cornerstone of treatment for the majority of patients with psoriasis, particularly those with limited disease.

The FDA-approved indications for the miscellaneous skin and mucous membrane agents are noted in Table 3 and Table 4. The pharmacokinetics, drug interactions, adverse drug events, as well as dosing and administration sections have been updated as necessary. The boxed warnings for acitretin, becaplermin, pimecrolimus, and tacrolimus are listed in Table 9 through Table 12. The boxed warning for oral acitretin relates to the birth defects caused by the use of this oral agent. The boxed warning for becaplermin states that there was an increased rate of mortality secondary to malignancy observed in patients treated with 3 or more tubes of becaplermin in a postmarketing retrospective cohort study. Use becaplermin only when the benefits can be expected to outweigh the risks and use with caution in patients with known malignancy. The boxed warnings for pimecrolimus and tacrolimus state that the long-term safety of topical calcineurin inhibitors has not been established. Rare cases of malignancy have been reported in patients treated with topical calcineurin inhibitors. Therefore, the continuous, long-term use of topical calcineurin inhibitors should be avoided and application should be limited to areas of involvement with atopic dermatitis.

Clinical studies evaluating the safety and efficacy of the miscellaneous skin and mucous membrane agents are summarized in Table 14. For the treatment of actinic keratoses, clinical trials have demonstrated a significant reduction in lesions with diclofenac, fluorouracil and imiquimod compared to placebo. Recently, three studies have been published. Diclofenac and imiquimod were found to be equally effective in a 12-week study conducted by Kose et al. Two studies evaluated the effects of fluorouracil and imiquimod in reducing actinic keratoses lesions. In the first study conducted by Tanghetti et al., fluorouracil was found to be more effective than imiquimod over a 24-week period. A second study conducted by Krawtchenko et al. demonstrated similar clearance rates with fluorouracil and imiquimod at the end of the active treatment phase; however, the 12 month sustained clearance rates were significantly higher with imiquimod compared to fluorouracil. For the treatment of atopic dermatitis, numerous clinical trials have demonstrated greater efficacy with pimecrolimus and tacrolimus compared to placebo. Several studies have also found tacrolimus to be more effective than pimecrolimus. For the treatment of basal cell carcinoma, imiquimod has been shown to be effective in both open-label and placebo-controlled studies. Fluorouracil has been shown to be effective in two studies; however, there are no placebo-controlled studies with this agent. For the treatment of cutaneous T-cell lymphoma, bexarotene has been shown to be effective in one open-label clinical trial, which evaluated its use in patients who were refractory to, intolerant to, or reached a response plateau for at least six months on at least two prior therapies. For the treatment of external anogenital warts, several clinical trials have demonstrated that both imiquimod and podofilox are effective treatments. A meta analysis of 12 placebo-controlled trials demonstrated similar clinical cure rates with imiquimod and podofilox. For the treatment of AIDS-related Kaposi's sarcoma, alitretinoin has been shown to be more effective than placebo in two clinical trials. For the treatment of psoriasis, numerous clinical trials have demonstrated that the combination product containing betamethasone/calcipotriene was more effective than monotherapy with betamethasone or calcipotriene. Several clinical trials have demonstrated similar efficacy with calcipotriene and tazarotene for the treatment of psoriasis.

Dr. Hisel concluded that the miscellaneous skin and mucous membrane class includes a diverse group of products used to treat many skin conditions. The wide variety of products, as well as the range of FDA-approved indications, makes direct comparisons difficult. It is important to analyze current treatment guidelines and published studies when making therapeutic decisions about the agents in this class. She summarized the recommendations from guidelines and highlighted the findings from clinical trials for each agent in this class as follows:

Guidelines for the management of actinic keratoses state that diclofenac, fluorouracil and imiquimod are effective and do not give preference to one agent over another. Several clinical trials have demonstrated a significant reduction in lesions with diclofenac, fluorouracil and imiquimod compared to placebo. Due to the limited number of comparative studies, it is difficult to make a direct comparison between these agents.

Guidelines for the treatment of atopic dermatitis state that topical corticosteroids are considered first-line therapy. Pimecrolimus and tacrolimus are second-line therapy for the short-term and non-continuous chronic treatment of atopic dermatitis in patients 2 years of age and older who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable. Several studies have found tacrolimus to be more effective than pimecrolimus. However, it should be noted that pimecrolimus is only indicated for the treatment of mild to moderate atopic dermatitis; whereas, tacrolimus is indicated for the treatment of moderate to severe atopic dermatitis. The long-term safety of topical calcineurin inhibitors has not been established. Although a causal relationship has not been established, rare cases of malignancy have been reported in patients treated with topical calcineurin inhibitors. Therefore, the long-term use of these agents should be avoided.

Guidelines for the treatment of superficial basal cell carcinoma recommend the use of fluorouracil and imiquimod in patients with low-risk squamous cell carcinoma in situ, where surgery or radiation is contraindicated or impractical and do not give preference to one agent over another. There are limited clinical trials evaluating the efficacy and safety of fluorouracil and imiquimod in the treatment of sBCC and there were no comparative studies found in the medical literature.

Guidelines for the treatment of cutaneous T-cell lymphoma state that bexarotene may be appropriate for patients with early stages (stage IA-IIA); however, patients with later stages (stage IIB or higher) will require systemic therapy. Bexarotene has been shown to be effective in one open-label clinical trial, which evaluated its use in patients who were refractory to, intolerant to, or reached a response plateau for at least six months on at least two prior therapies.

Guidelines for the treatment of anogenital warts state that there is no definitive evidence to suggest that any of the available treatments are superior to any other, and no single treatment is ideal for all patients or all warts. Several clinical trials have demonstrated that both imiquimod and podofilox are effective treatments and a meta analysis demonstrated similar clinical cure rates. However, no study has directly compared the efficacy and safety of these two agents. No clinical trials evaluating the use of podophyllum resin were found in the medical literature.

Guidelines for the treatment of hemorrhoids state that the cornerstone of therapy is adequate fiber intake and water. Topical corticosteroids and analgesics may bring symptomatic relief of local pain, itching and inflammation. Over-the-counter topical agents and suppositories are often used in the empirical treatment of hemorrhoids, however data supporting their use are lacking. A literature search did not reveal any published

studies evaluating the use of rectal products containing phenylephrine, shark liver oil, glycerin, mineral oil, and white petrolatum for the treatment of hemorrhoids.

Alitretinoin is the only miscellaneous agent indicated for the topical treatment of cutaneous lesions in patients with AIDS-related Kaposi's sarcoma. It has been shown to be more effective than placebo in two clinical trials. Alitretinoin should not be used when systemic therapy is required. There are no published guidelines available discussing the role of alitretinoin compared to other modalities for the treatment of Kaposi's sarcoma.

Guidelines for the management of psoriasis state that topical corticosteroids are the cornerstone of therapy for the majority of patients with psoriasis, particularly those with limited disease. Numerous clinical trials have demonstrated that the combination product containing betamethasone/calcipotriene was more effective than monotherapy with betamethasone or calcipotriene. However, no studies have been published which directly compare the betamethasone/calcipotriene combination product with dual use of betamethasone and calcipotriene as separate formulations. Several clinical trials have demonstrated similar efficacy with calcipotriene and tazarotene.

Collagenase is indicated for debriding chronic dermal ulcers and severely burned areas; however, there are few published studies available comparing its use with other agents or debridement techniques.

Guidelines on diabetic foot wound care state that becaplermin shows a modest benefit if used with adequate off-loading, debridement, and treatment of infection, but is not a substitute for comprehensive wound care. There are limited clinical trials assessing the efficacy and safety of becaplermin.

At this time, there is not a role for the miscellaneous skin and mucous membrane agents in general use. Because these agents have narrow indications with limited usage, they should be available for special needs and circumstances that require medical justification through the prior authorization process. After clinical circumstances are explored, proper medical justification will provide patient access to these agents.

There is insufficient data to support that one brand miscellaneous skin and mucous membrane agent is safer or more efficacious than another. Therefore, all brand miscellaneous skin and mucous membrane products within the class reviewed are comparable to each other and to the generics and offer no significant clinical advantage over other alternatives in general use.

No brand miscellaneous skin and mucous membrane agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

There were no further discussions on the agents in this class. Chairman Main asked the P&T Committee Members to mark their ballots.

6. NEW BUSINESS

Chairman Main stated that the August 2009 P&T Committee meeting was important as the members would be electing a new Vice-Chair (Chair-Elect). Dr. Culpepper will become the Committee's Chair beginning in November 2009.

7. RESULTS OF VOTE ANNOUNCED

Dr. Littlejohn announced the results of voting for each of the therapeutic classes and announced that all classes were approved as recommended. Results of voting are described in the Appendix to the minutes.

8. NEXT MEETING DATE

The next P&T Committee Meeting is scheduled for 9:00 a.m. on August 12, 2009 at the Medicaid Building in the Commissioner's Board Room. November 18, 2009 is the fourth meeting date for 2009.

9. ADJOURN

There being no further business, Dr. Woodruff moved to adjourn, and Ms. Faulk seconded.

The meeting was adjourned at 10:42 a.m.

Appendix

RESULTS OF THE BALLOTING
Alabama Medicaid Agency
Pharmacy and Therapeutics Committee
May 13, 2009

A. Recommendation: No brand skin and mucous membrane antibacterial is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Odell — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

B. Recommendation: No brand skin and mucous membrane antiviral is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Odell — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

C. **Recommendation:** No brand skin and mucous membrane antifungal is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

D. **Recommendation:** No brand skin and mucous membrane scabicide or pediculicide is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

E. Recommendation: No brand skin and mucous membrane miscellaneous local anti-infective is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

F. Recommendation: No brand skin and mucous membrane anti-inflammatory agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

G. **Recommendation:** No brand skin and mucous membrane antipruritic or local anesthetic is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

H. **Recommendation:** No brand skin and mucous membrane astringent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore MD — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

I. **Recommendation:** No brand skin and mucous membrane keratolytic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

J. **Recommendation:** No brand skin and mucous membrane keratoplastic agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

R Moore — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Medical Director

Kathy Hall — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Deputy Commissioner

Carol H. Steckel — ☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action
Commissioner

K. Recommendation: No brand miscellaneous skin and mucous membrane agent is recommended for preferred status. Alabama Medicaid should accept cost proposals from manufacturers to determine the most cost effective products and possibly designate one or more preferred brands.

Amendment: None

Vote: Unanimous to approve as recommended

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action

Medical Director

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action

Deputy Commissioner

☑ Approve ☐ Approve as amended ☐ Disapprove ☐ No action

Commissioner

Respectfully submitted,

Tina Hisel, Pharm.D., BCPS

May 13, 2009
Date